REMARKS

Reconsideration is requested.

In addition to the items requested in the paper filed April 17, 2009, the Examiner is requested to return an initialed copy of the previously filed PTO 1449 Form with the Examiner indicating that "International Search Report of PCT/GB2004/003273, mailed 3 November 2004" and "British Search Report dated December 23, 2003, issued in connection with GB 0318679.8" has been considered in a manner where same will be listed on the face of any patent issuing from the present application. The applicants acknowledge, with appreciation, the Examiner's indication on page 2 of the Office Action dated April 2, 2009, that the documents have been considered. The applicants note however that the Patent Office has regularly listed such documents on the face of issued U.S. Patents as notice within the issued patent of documents and information considered by the Examiner. The applicants note, for example, as evidence of the Patent Office practice in this regard, that the Patent Office has issued 102,125 patents since 1976 which contain the phrase "Search Report" as a description of documents listed under "Other References" on the face of issued patents. The following is a listing of the first 50 U.S. Patent Nos. and titles of patents obtained from a "Quick Search" of the U.S. Patent Office web site which met this criteria:

	PAT. NO.	Title
1	D601,242	Access device
2	D601,238	Filter cartridge
3	D601,172	Media device
4	7,596,804	Seamless cross-site user authentication status detection and automatic login

7,596,792 Method and system for supporting a plurality of event types
7,596,786 Method and apparatus for utilizing an existing product code to issue a match to a predetermined location on a global network
7,596,783 Methods and apparatus to implement annotation based thunking
7,596,767 System and process for controlling electronic components in a ubiquitous computing environment using multimodal integration
7,596,765 Sound feedback on menu navigation
7,596,760 System and method for selecting a tab within a tabbed browser
7,596,752 Delaying optimal paragraph layout during editing
7,596,730 Test method, test system and assist board
7,596,718 Ranged fault signatures for fault diagnosis
7,596,705 Automatically controlling processor mode of multi-core processor
7,596,701 Online data encryption and decryption
7,596,656 Memory cards with end of life recovery and resizing
7,596,645 Method for automatically adapting to the capabilities of a data-transmitting terminal and a device supplying data to said terminal requesting the data
7,596,644 Transmit rate pacing system and method
7,596,643 Storage subsystem with configurable buffer
7,596,637 Storage apparatus and control method for the same, and computer program product
7,596,631 Web browser of wireless device having serialization manager for maintaining registry of converters that convert data into format compatible with user interface of the device
7,596,627 Methods and apparatus for network congestion control
7,596,625 Peer-to-peer grouping interfaces and methods
7,596,622 Apparatus and method for processing web service descriptions
7,596,614 Network including snooping
7,596,609 WWW addressing
7,596,593 Methods and apparatus for efficiently transmitting interactive application data between a client and server using markup language
7,596,581 Relevance ranking of spatially coded documents
7,596,579 Method of reproducing an information storage medium having data structure for being reproduced adaptively according to player startup information
7,596,574 Complex-adaptive system for providing a facted classification
7,596,571 Ecosystem method of aggregation and search and related techniques
7,596,560 System and method for adaptive query identification and acceleration
7,596,552 Method and system for extracting web data
7,596,548 Query evaluation using ancestor information

35 7,596,535 T Apparatus for the classification of physiological events
36 7,596,531 T Method and apparatus for protecting against side channel attacks against personal identification numbers
37 7,596,523 T Method and apparatus for network-based portfolio management and risk-analysis
38 7,596,522 T Computer program product for fully insuring large bank deposits
39 7,596,520 T Systems and methods for general aggregation of characteristics and key figures
40 7,596,510 T Method, system and apparatus for requesting status information from a common carrier
41 7,596,466 T Inclination calculation apparatus and inclination calculation program, and game apparatus and game program
42 7,596,463 T Method and storage medium for calibrating a holographic storage system
43 7,596,459 T Apparatus and methods for multi-channel electric metering
44 7,596,458 T Tracking vibrations in a pipeline network
45 7,596,444 T Vehicle skid control device, automobile with vehicle skid control device mounted thereon, and vehicle skid control method
46 7,596,435 T Vehicle communication system and method with mobile data collection
47 7,596,432 T Method for estimating the food temperature inside a refrigerator cavity and refrigerator using such method
48 7,596,415 T Medical devices incorporating carbon nanotube material and methods of fabricating same
49 7,596,408 T Implantable medical device with anti-infection agent
50 7,596,403 T System and method for determining path lengths through a body lumen

The applicants note that the first U.S. utility patent listed above contains the following listed reference under "Other References": "International Search Report for PCT Application Serial No. PCT/US03/21244. cited by other". The second U.S. utility patent listed above contains the following listed reference under "Other References": "Search Report issued on Jan. 13, 2004 in counterpart foreign application in GB under application No. 317110.5. cited by other."

Further, the Examiner's Supervisor, Examiner Woitach, is listed as the Primary Examiner on the following 25 issued U.S. Patents where the phrase "Search Report" is contained in the list of "Other References":

	PAT. NO.	Title
1	7,393,683	Mammalian host cell modified by RNAi to inhibit .alpha. 1,6-fucosyltransferase
2	7,371,375	Protein
3	7,332,318	Calcium-independent phospholipases A.sub.2, genes thereof and promoter of the same
4	7,329,530	Chimaeric phages
5	7,312,058	Mutant serine acetyltransferase
6	7,309,602	Compositions and methods for producing fermentation products and residuals
7	7,285,413	Isolation tool for viable c-kit expressing cells
8	7,256,016	Recycling system for manipulation of intracellular NADH availability
9	7,252,943	In Vitro sorting method
10	7,241,744	Treating anemia in subjects by administration of plasmids encoding growth hormone releasing hormone
11	7,241,594	Gene encoding formate dehydrogenases D & E and method for preparing succinic acid using the same
12	7,186,812	Isolated human G-protein coupled receptors, nucleic acid molecules encoding human GPCR proteins, and uses thereof
13	7,172,893	Virus vectors and methods of making and administering the same
14	7,135,613	Chimeric gene constructs for generation of fluorescent transgenic ornamental fish
15	7,101,971	Erythropoietin analog-human serum albumin fusion
16	7,067,714	N-calcium channel knockout animal
17	7,067,308	Vector for genetically modifying non-human animals
18	7,053,187	Sperm-specific monoclonal antibody, mAbC
19	7,045,346	Nucleic acid constructs useful for glucose regulated production of human insulin in somatic cell lines
20	6,982,362	.alpha.-tocopherol transport protein knockout animal
21	6,939,711	Control of gene expression in plants by receptor mediated transactivation in the presence of a chemical ligand
22	6,916,603	Methods of using agents that modulate bone formation and inhibit adipogenesis
23	6,903,196	Methods for identifying and isolating tissue-specific lumen-exposed molecules
24	6,891,082	Transgenic non-human animals expressing a truncated activintype II receptor

25 6,878,692 T Apoptin-associating protein

The applicants note that the current Examiner is listed as the Primary Examiner on the following two (2) issued U.S. patents wherein the following "Search Reports" are listed on the face of the patents under "Other References":

PAT. NO.		Title
1	7,468,181 T	Means and methods for the production of adenovirus vectors
2	7,465,583 T	Duplexed parvovirus vectors

"PCT International Search Report, PCT/EP03/50125, dated Sep. 19, 2003. cited by other ." and "European Search Report, European Application No. EP 05076932.2, dated Mar. 17, 2006 (8 pages). cited by other .", respectively

Finally, the applicants note that the current Examiner is listed as the Assistant Examiner on the following two (2) issued U.S. patents wherein the following "Search Reports" are listed on the face of the patents under "Other References":

PAT. NO.		Title
1	7,125,695 T	Directed evolution of microorganisms
2	6,635,422 T	Methods for isolating and characterizing endogenous mRNA-protein (mRNP) complexes

"International Search Report for PCT/US00/13337. cited by other. " and "International Search Report for PCT/US00/35583, Apr. 18, 2001. ", respectively.

The applicants submit, with due respect, that the Patent Office has a history of listing information considered by the Examiner, including Search Reports, on the face of issued U.S. and Search Reports are not believed to be excluded under Rule 98.

Return of completely initialed PTO 1449 Forms, pursuant to MPEP § 609, is requested.

The specification has been revised in a manner suggested by the Examiner to obviate the objection to the drawings. Withdrawal of the objection to the drawings is requested.

The Examiner indicates on page 1 of the Office Action dated April 2, 2009 that none of the certified copies of the priority documents have been received. The Patent Office Image File Wrapper indicates however that a certified copy of the priority document has been received by the Patent Office. Specifically, the following "DO/EO WORKSHEET" is contained in the PTO IFW, without annotation:

DO/ EO WORKSHEET

Paralegal/ National Stage Division

U.S. Appl. No. 10/567453 International Appl. No. GB0403273

Application filed by : ☐ 20 months ☑ 30 months

WIPO PUBLICATION INFORMATION :

Publication No.: WO 2005/014800 Publication Language : ☑ English ☐ German ☐ Japanese ☐ Chinese ☐ Korean ☐ French ☐ Spanish ☐ Russian ☐ Other : _____

Publication Date : 17 02 05 Not Published : ☐ U.S. only designated ☐ EP request Published : ☐ EP request

INTERNATIONAL APPLICATION PAPERS IN THE APPLICATION FILE :

☑ International Application *(RECORD COPY)*
☐ Article 19 Amendments
☑ PCT/IPEA/489 IPER : ☑ EP ☐ JP ☐ SE ☐ AU ☐ US ☐ FR ☐ CN ☐ ES ☐ RU ☐ AT ☐ KR ☐ ___
☐ PCT/IPEA/409 IPER was NOT AVAILABLE at the time of paralegal review
☐ Annexes to 409
☑ Priority Document (s) No. 2

☐ PCT/IB/331
☐ Request form PCT/RO/101
☑ PCT/ISA/210 - Search Report : ☑ EP ☐ JP ☐ SE ☐ AU ☐ US ☐ FR ☐ CN ☐ ES ☐ RU ☐ AT ☐ KR ☐ OTHER ___ ☐ NONE
☐ Search Report References
☑ Other : 308

RECEIPTS FROM THE APPLICANT *(other than checked above) :*

☐ Basic National Fee *(or authorization to charge)*
☑ Description ☑ Claims ☑ Abstract
☑ Drawing Figure(s) - (# of drwgs. 14)
☐ Translation of Article 19 Amendments ☐ entered ☐ not entered : ☐ not a page for page substitution ☐ replaced by Article 34 Amendment
☐ Annexes to 409 ☐ entered ☐ not entered : ☐ not a page for page substitution ☐ no translation ☐ other : _____
☐ Application Data Sheet
☐ Power of Attorney/ Change of Address

☑ Preliminary Amendment(s) Filed on : 1. _____ 2. _____ 3. _____
☑ Information Disclosure Statement(s) Filed on : 1. _____ 2. _____ 3. _____
☐ Assignment Document *(forwarded to Assignment Branch)* 1. _____
☐ Assignee PG Publication Notice
☐ Substitute Specification Filed on : 1. _____ 2. _____
☐ Verified Small Status Statement 1. _____
☑ Oath/ Declaration (executed) 18 July 2006 ☐ unsigned ☐ no citizenship
☐ DNA Diskette ☐ Sequence Listing
☐ Other : _____

NOTES : ☐ I.A. used as Specification ☐ Other :

35 U.S.C. 371 - Receipt of Request (PTO-1390)	07 February 2006
Date Acceptable Oath/ Declaration Received	18 July 2006
Date of Completion of requirements under 35 U.S.C. 371	1
Date of Completion of ALL requirements	18 July 2006
Date of Completion of DO/ EO 903 - Notification of Acceptance	01 November 2006
Date of Completion of DO/ EO 905 - Notification of Missing Requirements	
Date of Completion of DO/ EO 909 - Notification of Abandonment	
Date of Completion of DO/ EO 916 - Notification of Defective Response	
Date of Completion of DO/ EO 922 - Notification to Comply w/ Requirements for Patent Applications Containing Nucleotide and/or Amino Acid Sequence Disclosures	
Date of Completion of DO/ EO 923	

The Examiner is requested to confirm receipt of the priority documents in a further paper.

Claims 1-16, 33-41 and 43-50 are pending.

Claims 1 and 10 have been revised in a manner suggested by the Examiner to obviate the objection to same. Withdrawal of the objection to claims 1 and 10 is requested.

The Section 102 rejection of claims 1, 4-11, 14-16, 33, 34, 37-41, 43 and 46-50 over Field (U.S. Patent No. 6,593,140), is traversed. While claim 42 has been rejected over Field under Section 102, the claim was canceled, without prejudice, in the Preliminary Amendment filed February 7, 2006. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Examiner asserts that the medium used in example 5 was serum-free, citing example 2 as evidence. However, example 5 is silent regarding the presence or absence of serum, the media is characterized only by the presence of transferrin or tropolone with 0.2mg/l ferric ammonium citrate, or by presence of 0.2mg/l ferric ammonium citrate in the absence of transferrin or tropolone.

Field describe use of the lipophilic iron chelator tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one), particularly in agitated cell culture.

> "We have now found that 2-hydroxy-2,4,6-cycloheptatrien-1-one meets all of these criteria and may be used advantageously in animal cell culture to support the growth of cells. In particular, we have found that its use can support growth in agitated cell culture, where it is necessary to use low iron concentration to avoid toxicity problems, and where

> the use of other recognised chelating agents such as citrate and gluconate has failed."

Example 5 discloses that a medium containing 0.2 mg/l ferric ammonium citrate did not support the growth of mouse myeloma cells as the myeloma cells:

> "…failed to thrive and died within 48 hours"

Thus Field *et al.* (which corresponds to WO 94/02592, acknowledged in the background of the present application) do not disclose growth of mouse myeloma cells in agitated suspension culture the presence of low concentrations of iron, unless transferrin or tropolone is present.

In contrast, the present inventors have demonstrated that a medium containing low concentrations of iron is capable of supporting the growth of a myeloma cell line in methods and processes involving agitated suspension culture in the absence of transferrin or a chelator such as tropolone.

The method and process of the claims are not anticipated by Field and wwithdrawal of the Section 102 rejection is requested.

The Section 102 rejection of claims 1-7, 33-41 and 43-50 over Gorfien (U.S. Patent Application Publication No. 2006/0148074), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

Gorfien is derived from WO98/08934, which is acknowledged in the present specification. Gorfien discloses culture of cells in replacement media "1x medium" ¶[0137] in which animal proteins, transferrin or insulin, are replaced with ferrous sulphate chelate ¶[0137]; the preferred ferrous sulphate chelate being the nitrogen-containing chelate ferrous sulphate EDTA (¶[0113], Example 2). Use of ferric citrate in

the form of $FeCl_3$ -sodium citrate is mentioned but this was required at a higher concentration than the ferrous sulphate EDTA (Example 2). Gorfien disclose that low iron concentrations can be used for growth of certain mammalian cells but only when iron is present as a chelate with a nitrogen-containing chelating compound, such as EDTA. The presence of such nitrogen-containing chelators is specifically excluded from the media used in the methods and processes of the present invention.

Accordingly, Gorfien is not believed to disclose methods and processes according to the presently claimed invention. Withdrawal of the Section 102 rejection is requested.

The Section 103 rejection of claims 1-16, 33-41 and 43-50 over Field in view of Gorfien is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Gorfien desire to produce a replacement medium free from animal proteins such as transferrin (see ¶[0032]). At ¶[0112], Gorfien state that:

> "In accordance with the invention, transferrin is replaced with iron or an iron-containing compound and/or insulin is replaced with zinc or a zinc containing compound. Preferably, iron chelate compounds are used in accordance with the invention."

When culture of myeloma cells is discussed, Gorfien teach media ("1x medium", supplemented with a lipid mixture) for culturing NS/O myeloma cells (see ¶[0144]). It is stated that the "iron chelate compound" is preferably added to the 1x medium prior to filter sterilization see, e.g. ¶[0138], ¶[0141].

Thus, Gorfien teach that iron be provided in the form of an iron chelate compound as described in ¶[0113]:

> " [0113] Fe^{2+} and/or Fe^{3+} chelate compounds which may be used include but are not limited to compounds containing an Fe^{2+} and/or Fe^{3+} salt and a chelator such as ethylenediaminetetraacetic acid (EDTA), ethylene glycol-bis(β-aminoethyl ether)-N,N,N,N'-tetraacetic acid (EGTA), deferoxamine mesylate, dimercaptopropanol, diethylenetriaminepentaacetic acid (DPTA), and trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (CDTA). For example, the iron chelate compound may be a ferric citrate chelate or a ferrous sulfate chelate. Preferably, the iron chelate compound used is ferrous sulphate.$7H_2O$ EDTA ($FeSO_4.7H_2O$ EDTA, e.g., Sigma F0518, Sigma, St. Louis, Mo.). In the medium of the present invention, the concentration of Fe^{2+} and/or Fe^{3+} can be optimized using only routine experimentation. Typically, the concentration of Fe^{2+} and/or Fe^{3+} in the 1x medium of the present invention can be about 0.00028 to 0.011 g/L. Preferably, the concentration of iron is about 0.0011 g/L."

Gorfien do not teach the use of ferric ammonium citrate.

The Examiner asserts that it would have allegedly been obvious to one of ordinary skill in the art at the time the invention was made to use ferric ammonium citrate as taught by Field in the media taught by Gorfien. The applicants respectfully disagree with the Examiner's conclusion and consideration of the following in this regard is requested.

Field is not a predictable starting point for those of ordinary skill in the art seeking to culture myeloma cells in the absence of transferrin or tropolone (a lipophilic iron chelator) as required by the present claims.

Field discloses that a medium containing 0.2 mg/l ferric ammonium citrate, in the absence of an iron chelator (transferrin or tropolone), did not support the growth of

mouse myeloma cells, as the myeloma cells: "…failed to thrive and died within 48 hours" (Example 5).

Thus, Field teaches away from use of ferric ammonium citrate in the absence of an iron chelator.

The stated aim of Gorfien is to produce a replacement medium free from animal proteins such as transferrin (see ¶[0032]). One of ordinary skill in the art combining Gorfien with the teaching of Field would have been directed, at best, to have modified the media taught by Gorfien to include ferric ammonium citrate and the lipophilic iron chelator tropolone, because Field teach that a medium containing ferric ammonium citrate does not support myeloma cell growth unless either transferrin or tropolone is present.

The methods and processes claimed require culture of myeloma cells in the absence of transferrin or a lipophilic iron chelator such as tropolone. The applicants respectfully submit therefore that the claimed invention would not have been obvious over Field and Gorfien, considered individually, or in combination.

Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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